JANSSEN-CILAG GmbH

Final Clinical Study Report

A prospective, multicentric, non-interventional study in Germany: Insight into therapy, routine safety, quality of life, and pharmacoeconomic outcomes in patients with active psoriasis arthritis being treated with ustekinumab in daily clinical practice

SUSTAIN

Protocol CNTO1275PSA4002; Non-interventional study

CNTO1275 Ustekinumab (Stelara®)

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DATE STUDY INITIATED: 24-FEB-2015 (first subject in)

DATE STUDY COMPLETED: 04-MAY-2020 (last subject out)

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Prepared by: JANSSEN-CILAG GmbH
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GCP Compliance: This study was conducted in compliance with Good Clinical Practice, including the archival of essential documents.

SYNOPSIS

Name of Sponsor/Company	JANSSEN-CILAG GmbH
Name of Medicinal Product	CNTO1275 Ustekinumab (Stelara®)

Status:	Approved
Date:	11 May 2021
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Protocol No.: CNTO1275PSA4002

Title of Study: A prospective, multicentric, non-interventional study in Germany: Insight into therapy, routine safety, quality of life, and pharmacoeconomic outcomes in patients with active psoriasis arthritis being treated with ustekinumab in daily clinical practice

Study Name: SUSTAIN

NCT No.: N/A

Clinical Registry No.: PEI NIS No. 290

Coordinating Investigator(s): Jörg Wendler, M.D., Möhrendorfer Straße 1c, Erlangen, Germany

Study Center(s): 75 sites located in Germany

Publication (Reference): None

Study Period: 24-FEB-2015 (first subject in) to 04-MAY-2020 (last subject out)

Phase of Development: Not applicable, since this is a non-interventional study (NIS).

Objectives: This NIS aimed to investigate prospectively the long-term efficacy and long-term safety of ustekinumab as well as its influence on quality of life and other patient-reported outcomes (PRO) in subjects with active psoriatic arthritis (PsA) in routine care.

Methodology: This was a non-interventional, single group, observational study conducted at multiple sites in Germany that evaluated ustekinumab in subjects with PsA. The planned total sample size was approximately 400 subjects. The planned observation period per subject was about 3 years (160 weeks). If therapy with ustekinumab was not continued, NIS-related documentation should be ended (termination documentation). This study was based on a non-interventional design. This means that physician and subject did not follow a previously stipulated diagnostic and therapeutic schedule; rather, the non-influenced treatment routine had priority, followed by its standardized documentation.

The subject should visit the treating physician for the ustekinumab injections at Week 0, 4 and then every 12 weeks thereafter according to the prescribing information. A visit window of +/-4 weeks was intended for deviations from routine.

Number of Subjects (planned and analyzed): The planned total sample size was approximately 400 subjects. Last subject in for the study was on 30-MAR-2017 with in total 337 enrolled subjects. Documentations were available for 337 (100.0%) at baseline, 311 subjects (92.3%) at Week 4, 319 (94.7%) at Week 16, 282 (83.7%) at Week 28, 242 (71.8%) at Week 40, 216 (64.1%) at Week 52, 189 (56.1%) at Week 64, 164 (48.7%) at Week 76, 157 (46.6%) at Week 88, 153 (45.4%) at Week 100, 146 (43.3%) at Week 112, 134 (39.8%) at Week 124, 134 (39.8%) at Week 136, 123 (36.5%) at Week 148, and 129 (38.3%) at Week 160.

Diagnosis and Main Criteria for Inclusion: Male and female subjects who were at least 18 years old with a confirmed diagnosis of an active PsA and inadequate response to previous therapy with disease modifying anti-rheumatic drugs (DMARDs) who were intended for ustekinumab therapy according to the physicians' decision were eligible for this study after having signed the informed consent form prior to the start of documentation.

Subjects who participated in other clinical drug trials during the observation period had to be excluded from documentation. Also excluded from documentation were subjects who were treated with another biological agent apart from ustekinumab in the PsA indication. In addition, the contraindications mentioned in the prescribing information had to be heeded.

Test Product, Dose and Mode of Administration, Batch No.: The treatment was to be performed according to the Summary of Product Characteristics (SmPC) based on the individual subjects' needs and on the site physicians' decision (non-interventional study design). Ustekinumab was commercially available in a pre-filled syringe (45 mg/0.5 mL and 90 mg/1.0 mL dosage) and injected subcutaneously in the abdominal region or thigh.

Reference Therapy, Dose and Mode of Administration, Batch No.: Not applicable.

Duration of Treatment: The planned observation period per subject was about 3 years (160 weeks). If therapy with ustekinumab was not continued, the NIS-related documentation should be ended (termination documentation).

Criteria for Evaluation: The following effectiveness parameters were evaluated for this final analysis: course of number of tender and swollen joints, course of Body Surface Area (BSA) affected by psoriasis and Psoriasis Activity and Severity Index (PASI), the PsA modified Maastricht ankylosing spondylitis enthesitis score (MASES), course of subjects' assessment of disease activity (visual analogue scale = VAS), subjects' assessment of pain (VAS), subjects' assessment of sleep quality (VAS), and course of Health Assessment Questionnaire-Disability Index (HAQ-DI), course of subjects' and physicians' assessment of effectiveness, subjects' Minimal Disease Activity (MDA), course of SF-12, course of Bath Ankylosing Spondylitis Disease Activity Index (BASDAI), course of Nail Psoriasis Severity Index (NAPSI), and course of dactylitis score, and uveitis. Safety was assessed by the incidence of adverse events (AEs) and serious AE (SAEs), subjects' and physicians' global tolerability assessment and by the course of C-reactive protein (CRP) and erythrocyte sedimentation rate (ESR).

Statistical Methods: The NIS was analyzed using primarily descriptive statistical methods. The collected data were described, depending on type of characteristic, by mean, variance, minimum, maximum and median, or based on frequency distributions. 95% confidence intervals (CIs) were given for the mean numbers and changes from baseline in tender and swollen joint counts. Data measured several times during the study were analyzed by visit presenting absolute and relative differences to baseline for numerical data. Missing values were not replaced.

RESULTS:

STUDY POPULATION:

The only data set analyzed for this analysis was the full analysis set (FAS), which included all subjects who were treated with ustekinumab and documented within the study including all data up to Week 160. By end of the study, 337 subjects (100.0%) had a baseline documentation; follow-up documentations were available for 311 subjects (92.3%) at Week 4, 319 (94.7%) at Week 16, 282 (83.7%) at Week 28, 242 (71.8%) at Week 40, 216 (64.1%) at Week 52, 189 (56.1%) at Week 64, 164 (48.7%) at Week 76, 157 (46.6%) at Week 88, 153 (45.4%) at Week 100, 146 (43.3%) at Week 112, 134 (39.8%) at Week 124, 134 (39.8%) at Week 136, 123 (36.5%) at Week 148, and 129 (38.3%) at Week 160.

A total of 146 subjects (43.3%) had discontinued ustekinumab treatment, mostly due to loss of efficacy (45 subjects, 13.4%) or lack of efficacy (39 subjects, 11.6%). Other reasons for premature discontinuation were patient's wish (15 subjects, 4.5%), adverse event (13 subjects, 3.9%), worsening of PsA (12 subjects, 3.6%), worsening of PsO (8 subjects, 2.4%), lack of compliance (1 subject, 0.3%) and other reasons (13 subjects, 3.9%.

Of the 337 subjects enrolled, 145 (43.0%) were males and 192 (57.0%) were females. Subjects' mean (SD) age was 53.6 (10.8) years. Subjects' mean (SD) age at first manifestation of skin and musculoskeletal symptoms was 31.5 (15.7) years and 41.6 (12.8) years, respectively. Almost all subjects (97.0%, 327 subjects) had received prior medications for PsA treatment, mostly (in more than 30% of subjects) MTX (79.5%, 268 subjects), adalimumab (37.1%, 125 subjects), prednisone/prednisolone (32.6%, 110 subjects) and leflunomide (30.3%, 102 subjects).

With regard to type of prior DMARD treatment, a total of 327 subjects (97.0%) had received at least one prior DMARD, with 318 subjects (94.4%) having received at least one conventional DMARD (cDMARD), 183 subjects (54.3%) having received at least one TNF inhibitor, and 10 subjects (3.0%) having received at least one other (non-TNF inhibitor) biologic. 152 subjects (45.1%) had neither received TNF inhibitors nor other biologics for the treatment of their PsA.

With regard to the number of prior TNF inhibitors per subject, 154 subjects (45.7%) were TNF inhibitor naïve, 87 subjects (25.8%) had received 1 prior TNF inhibitor, 59 subjects (17.5%) had received 2 prior TNF inhibitors, and 37 subjects (11.0%) had received ≥3 prior TNF inhibitors (please note: although 2 of these 154 subjects were TNF-naïve, they had received another biologic pre-treatment. Thus, they were no counted in the group of subjects with neither TNF-inhibitor nor biologic pre-treatment as reported in the preceding paragraph [N=152]).

Most subjects received ustekinumab at a dose of 45 mg dose (242 subjects, 72.0%), while the 90 mg dose was administered to 94 subjects (28.0%).

EFFECTIVENESS RESULTS:

Tender and swollen joint counts: From baseline to Week 28, average values of TJC and SJC markedly decreased under treatment with ustekinumab, with first improvements already seen at Weeks 4 and 16. In parallel, mean tender and swollen joint count of small peripheral joints also decreased. Baseline values of mean TJC and SJC of large joints were low and, consequently, only slight absolute improvements could be observed. A sustained positive effect was indicated in subjects who continued treatment beyond Week 28 through Week 160. The 95%-CIs for all mean changes in the joint counts consistently excluded the 0 value across all visits, thereby indicating nominally significant improvements based on an exploratory alpha level (2-sided) of 5% (see following synopsis table of effectiveness).

Course of TJC, SJC, small peripheral TJC and SJC, large TJC and SJC and changes from baseline over 160 weeks of treatment with ustekinumab (FAS)

	Baseline Mean [95%-CI]; Median	Week 28 Mean [95%-CI]; Median	Week 52 Mean [95%-CI]; Median	Week 100 Mean [95%-CI]; Median	Week 160 Mean [95%-CI]; Median
TJC analyses	n=325	n=269	n=208	n=145	n=122
TJC	10.0 [8.6; 11.3]; 6.0	4.1 [3.2; 4.9]; 1.0	3.6 [2.7; 4.6]; 0.0	1.8 [1.2; 2.4]; 0.0	1.0 [0.6; 1.4]; 0.0
Change from BL	n.a.	-5.8 [-7.3; -4.3]; -3.0	-5.6 [-7.0; -4.1]; -3.0	-6.5 [-7.9; -5.1]; -5.0	-7.0 [-8.5; -5.5]; -5.0
Small peripheral TJC	7.6 [6.4; 8.7]; 4.0	2.8 [2.1; 3.6]; 0.0	2.8 [2.0; 3.6]; 0.0	1.3 [0.8; 1.8]; 0.0	0.7 [0.3; 1.0]; 0.0
Change from BL	n.a.	-4.6 [-5.9; -3.3]; -2.0	-4.2 [-5.4; -2.9]; -2.0	-5.1 [-6.4; -3.8]; -3.0	-5.5 [-6.9; -4.1]; -3.0

Course of TJC, SJC, small peripheral TJC and SJC, large TJC and SJC and changes from baseline over 160 weeks of treatment with ustekinumab (FAS)

	Baseline Mean [95%-CI]; Median	Week 28 Mean [95%-CI]; Median	Week 52 Mean [95%-CI]; Median	Week 100 Mean [95%-CI]; Median	Week 160 Mean [95%-CI]; Median
Large TJC	1.8 [1.5; 2.0]; 1.0	0.9 [0.7; 1.1]; 0.0	0.6 [0.4; 0.7]; 0.0	0.4 [0.2; 0.6]; 0.0	0.3 [0.1; 0.4]; 0.0
Change from BL	n.a.	-0.9 [-1.1; -0.6]; 0.0	-1.1 [-1.3; -0.8]; 0.0	-0.9 [-1.2; -0.7]; 0.0	-1.1 [-1.4; -0.8]; -1.0
SJC analyses	n=321	n=269	n=208	n=145	n=122
SJC	4.1 [3.4; 4.9]; 2.0	1.8 [1.2; 2.3]; 0.0	1.3 [0.8; 1.8]; 0.0	0.6 [0.3; 0.9]; 0.0	0.4 [0.2; 0.6]; 0.0
Change from BL	n.a.	-2.4 [-3.2; -1.6]; -1.0	-2.9 [-3.7; -2.0]; -1.0	-4.3 [-5.4; -3.1]; -2.0	-4.1 [-5.2; -2.9]; -2.0
Small peripheral SJC	3.4 [2.7; 4.1]; 1.0	1.4 [0.9; 1.8]; 0.0	1.1 [0.6; 1.6]; 0.0	0.5 [0.2; 0.7]; 0.0	0.3 [0.1; 0.5]; 0.0
Change from BL	n.a.	-2.0 [-2.8; -1.3]; 0.0	-2.4 [-3.2; -1.6]; 0.0	-3.8 [-4.9; -2.7]; -1.0	-3.6 [-4.7; -2.5]; -1.0
Large SJC	0.5 [0.4; 0.6]; 0.0	0.3 [0.2; 0.4]; 0.0	0.2 [0.1; 0.2]; 0.0	0.1 [0.0; 0.2]; 0.0	0.1 [0.0; 0.1]; 0.0
Change from BL	n.a.	-0.2 [-0.3; -0.1]; 0.0	-0.3 [-0.4; -0.2]; 0.0	-0.3 [-0.4; -0.2]; 0.0	-0.3 [-0.5; -0.2]; 0.0

BL = Baseline; CI = Confidence interval; FAS = Full analysis set; TJC = Tender joint count; SJC = Swollen joint count; n=Number of observations; n.a. = not applicable.

In all subgroup analyses (i.e. subgroups by prior treatment, subgroups by concomitant methotrexate treatment, subjects with axial involvement, subjects with dactylitis), a decrease in TJC and SJC was also seen as compared to all analyzed subjects. Regarding the subgroups by prior treatment, the highest impact under ustekinumab was observed in subjects pre-treated with 1 or 2 biologics.

Skin symptoms and enthesitis: 10.0% of the BSA (median value) were affected at baseline. BSA affected decreased by median -5.0% at Week 28, and this improvement was sustained over time through Week 160 (6.5% at Week 52, 7.0% at Week 76, and 7.0% at Week 100, -8.0 at Week 124, -7.0 at Week 160). PASI declined from median of 4.8 at baseline to median 0.0 at Week 160 (median decrease by -5.1), corresponding to a continued improvement.

From baseline through Week 160, the median MASES was 0.0 at all visits and mean values rather small, indicating that there was, on an average, no clinically relevant enthesitis activity measured throughout the course of the study.

Comparable results were observed in the subgroup analyses (i.e. subgroups by prior treatment, subgroups by concomitant MTX treatment, subjects with axial involvement, subjects with dactylitis).

Patient-reported outcomes: At all study visits, subjects were asked to assess global disease activity, pain, and sleep quality on a 100 mm VAS, and to complete the HAQ-DI patient questionnaire. The median disease activity at baseline was 60.0 mm and decreased continuously to median 43.5 mm at Week 28 (by -12.0 mm) and 30.0 mm at Week 160 (by -18.0 mm). Similarly, the median value for the perceived pain intensity at baseline was 61.0 mm and decreased continuously to median 45.0 mm at Week 28 (by -6.0 mm) and 30.0 mm at Week 160 (by -17.0 mm).

Median value of sleep quality VAS was 42.0 mm at baseline, and the mean/median increases (i.e. improvements) at all post-baseline visits were rather slight. Median improvements were by 1.0 mm at Week 28 and 5.0 mm at Week 160.

With regard to HAQ-DI, a trend towards functional improvement was noted, but the post-baseline changes were slight, and the extent of mean improvements did not fulfill the definition of a minimum clinically

important change (i.e., changes from baseline by at least -0.3 score points). The median HAQ-DI at baseline was 1.000, and a subsequent decrease was seen by -0.125 at Week 28 and by -0.250 at Week 160.

Subgroup analyses:

Mean baseline values of disease activity were higher, the more prior biologics had been used, ranging from 54.1 mm in subjects not pre-treated with any biologic to 62.4 mm in subjects pre-treated with >2 biologics. In all 4 subgroups by prior therapy, a decrease in disease activity was observed up to Week 160, but also graded by number of prior therapies with mean values ranging from 29.0 mm in subjects not pre-treated to 48.6 mm in subjects pre-treated with >2 biologics.

Similar to the assessment of disease activity, subjects' assessment of pain at baseline increased with the number of prior treatments with biologics. During the study, pain assessment decreased in all subgroups by prior therapy (54.4 mm in subjects not pre-treated and 61.2 mm in subjects pre-treated with >2 biologics), however, not to the same extent(mean decrease by -21.0. mm in subjects not pre-treated and mean decrease by -16.2 mm in subjects pre-treated with >2 biologics).

Sleep quality was assessed better by subjects the less prior treatment they had received (mean values of 48.1 mm in subjects not pre-treated and 37.4 mm in subjects pre-treated with >2 biologics). In all subgroups, sleep quality increased up to Week 160 in all subgroups (64.4 mm in subjects not pre-treated and 54.9 mm in subjects pre-treated with >2 biologics). HAQ-DI was also higher in subjects with more prior treatments at baseline, followed by decreases in all subgroups (from 0.896 to 0.592 in subjects not pre-treated and from 1.255 to 1.036 in subjects pre-treated with >2 biologics).

At baseline, subjects without concomitant MTX treatment assessed their disease activity higher (mean of 59.9 mm) than subjects concomitantly receiving MTX (mean of 53.9 mm). In both subgroups, disease activity decreased during the study up to Week 160 (37.6 mm in subjects without MTX and 29.7 mm in subjects with MTX). The effect of ustekinumab treatment on pain and sleep quality was higher in subjects concomitantly treated with MTX (decreases in pain by -18.2 vs. -21.1 in subjects without vs. with MTX; increases in sleep quality by 8.4 vs. 10.4 in subjects without vs. with MTX).

Global effectiveness assessments: At Week 52 (after the first treatment year), the global effectiveness of ustekinumab was assessed as "very good" or "good" by 85.3% (175/205) of physicians and by 82.8% (164/198) of study subjects. These favorable results of the effectiveness assessment were maintained and even improved during the course of the study, as the corresponding proportions were 93.2% (137/147) and 92.4% (134/145), respectively, at Week 100, and 94.1% (113/120) and 89.8% (106/118), respectively, at Week 160. In all subgroups, assessments of effectiveness by physicians and subjects was high throughout the study.

Rate of subjects with MDA: The rate of subjects with MDA at Week 28 and Week 52 was based on subjects without MDA at baseline (N=292). MDA was reached by 55 subjects (18.8%) at Week 28 and by 52 subjects (17.8%) at Week 52. Median time until a subject reached MDA was 64 weeks [46.3; 78.1]. Regarding the subgroups by prior therapy, considerably more of the subjects not pre-treated with biologics reached MDA at Weeks 28 and 52. The values in the other subgroups were comparably low (≤10%). Subgroups by concomitant MTX treatment, with axial involvement or dactylitis were comparable to all subjects regarding achievement of MDA.

Course of SF-12: Physical summary scale and mental health summary scale increased by median 5.7 points and 3.1 points at Week 160, respectively, showing a slight improvement under ustekinumab.

Course of BASDAI: A slight improvement from baseline to Week 160 by median -1.9 points could be observed. However, the questionnaire was filled in by only a small number of subjects (N=6 at Week 160).

Course of NAPSI: The median NAPSI score at baseline was 4.0, mean (SD): 14.3 (23.1) and improved continuously to median 0.0, mean (SD) 6.5 (19.4) at Week 160.

Course of dactylitis score: Median dactylitis score was 0.0 at all timepoints. The mean (SD) dactylitis score decreased from 1.7 (5.4) at baseline to 0.3 (1.8) at Week 160, corresponding to a mean (SD) change by -1.1 (3.6).

Subgroup analyses by prior therapy, concomitant MTX treatment, subjects with axial involvement and subjects with dactylitis showed comparable results to the analysis of all subjects with regard to mean decreases in dactylitis score from baseline to Week 160. .

Socio-economic parameter: Although an improvement of PsA could be observed throughout the study, early retirement due to PsA increased from baseline (70.1%) to Week 160 (92.0%). In parallel, the percentage of employment decreased slightly from 58.2% at baseline to 55.6% at Week 160. The mean (SD) number of total working hours increased slightly from 31.1 (14.4) at baseline to 33.1 (13.4) at Week 160 and accordingly, the number or working hours missed was decreasing during the study from 2.9 (9.6) at baseline to 0.8 (5.7) at Week 160.

SAFETY RESULTS:

Summaries of AEs and other safety data are based on the 337 study subjects who were included in the FAS. A total of 282 subjects (83.7%) experienced at least one AE until the current cut-off date, with 194 subjects (57.6%) experiencing AEs that were regarded by the reporting physician as related to ustekinumab. The following synopsis table of safety provides a concise overview of the adverse event experience until the current cut-off date for analysis.

Summary of AEs (FAS)

Parameter	All subjects, (N=337)
Number (%) of subjects	
At risk	337 (100.0)
With AE	282 (83.7)
With AE related to ustekinumab [a]	194 (57.6)
With AE related to MTX [a]	100 (29.7)
With SAE	55 (16.3)
With SAE related to ustekinumab [a]	12 (3.6)
With SAE related to MTX [a]	5 (1.5)
Number (%) of events	
All AE	1083 (100.0)
AE related to ustekinumab [a]	392 (36.2)
AE related to MTX [a]	166 (15.3)
SAE	96 (8.9)
SAE related to ustekinumab [a]	16 (1.5)
SAE related to MTX [a]	6 (0.6)

[a] "Related" events are events with missing, possible, likely or very likely causality.
AE = Adverse event; MTX = methotrexate; SAE = Serious adverse event.

The highest AE incidences (>20.0% of study subjects) were seen within the primary MedDRA SOCs "general disorders and administration site conditions" (36.5%, 123 subjects), "infections and infestations" (36.5%, 123 subjects), "musculoskeletal and connective tissue disorders" (30.9%, 104 subjects), and "injury, poisoning and procedural complications" (24.6%, 83 subjects).

According to the observational plan V4.0, some events requiring a special reporting situation were defined. Among these events, "off label use" (e.g. overdose) and "drug ineffective" were listed. These events were reported as AE in the eCRF.

The most common AEs (≥3.0% or 10 subjects) at the preferred term level were: "nasopharyngitis" and "off label use"[a] (19.3%, 65 subjects), "drug ineffective"[b] (19.0%, 64 subjects), "psoriatic arthropathy" (10.1%, 34 subjects), “therapeutic product effect decreased” (8.9%, 30 subjects), "arthralgia" (5.6%, 19 subjects), "cough" (5.0%, 17 subjects), "diarrhoea" (4.5%, 15 subjects), "psoriasis" (3.6%, 12 subjects), "bronchitis", "gastrointestinal infection", "vitamin D deficiency" (3.3%, 11 subjects), and "fatigue", and "hypertension" (3.0%, 10 subjects each).

A total of 55 subjects (16.3%) experienced at least one SAE until the study end. The pattern of SAE was quite diverse. The highest incidences were seen in SAEs pertaining to the MedDRA SOC "musculoskeletal and connective tissue disorders" (22 subjects, 6.5%). "psoriatic arthropathy" (6 subjects, 1.8%), "intervertebral disc protrusion", "atrial fibrillation" and "syncope" (3 subjects, 0.9%, each), "abscess limb", "arthralgia", "lumbar spinal stenosis", "osteoarthritis", "pain", "cellulitis", "coronary artery disease", and "ovarian cyst" (2 subjects 0.6% each). All other SAE occurred in single subjects only.

A total of 16 SAEs occurring in 12 subjects (3.6%) were assessed by investigators as at least possibly related to ustekinumab treatment. Most of the drug-related SAEs were associated with worsening of PsA (6 subjects) or other joint complaints (one subject each with RA flare and arthralgia plus joint swelling). Drug-related SAEs not manifesting at the joints (seen in 4 subjects) were thrombosis, pneumonia, myelitis, and breast cancer plus breast calcification (one subject each).

Four subjects were reported with malignancies (breast cancer, Hodgkin’s disease, rectal cancer, and squamous cell carcinoma of the cervix). These events were assessed as unrelated to treatment with ustekinumab. No other SAEs pertaining to the watchlist events were documented.

Five subjects died during the course of the study. The fatal events reported were: cerebrovascular accident, pulmonary embolism, death (unknown reason), cardiac failure, and road traffic accident; all events were assessed as unrelated or unlikely related to ustekinumab treatment.

The vast majority of physicians and subjects assessed the tolerability of ustekinumab as very good or good throughout the course of the study (98.2% of physicians and 97.7% of subjects at Week 28, 99.2% of physicians and 100% of subjects at Week 160).

STUDY LIMITATIONS: Generally, the risk of selection/ascertainment bias and the lack of a parallel control group, which complicate the interpretation of the causality between treatment and outcomes, are inherent limitations of non-interventional, observational studies. In addition, no imputation methods for the data of subjects who have discontinued the study are applied, thereby resulting in the potential risk of a positive selection of subjects with a favorable treatment response especially in the later phases of the study (attrition bias).

CONCLUSION(S):

The results of the final analysis based on the non-interventional study data through 160 weeks of treatment suggest that ustekinumab used in routine care is an effective PsA treatment for managing both aspects of the disease, i.e., musculoskeletal as well as skin manifestations. The clinical improvements seen upon the objective medical examinations were accompanied by improvements in patient-reported outcomes (disease activity and pain assessment). An early onset of efficacy was seen as of week 4 or week 16. Moreover, long term efficacy was observed, i.e. stable response until the last week of documentation (Week 160). In addition, the rate of subjects with early termination due to lack of efficacy decreased over time. However,

[a] If a higher ustekinumab dose regarding body weight was used than recommended by the SmPC (i.e. 90 mg in subjects < 100 kg), this had to be documented as off-label use in the eCRF.

[b] Drug ineffective had to be documented as AE in the eCRF.

due to the accumulating number of discontinuing subjects that resulted in missing data over time, the effectiveness results should be interpreted with caution.

Clinical improvements were also observed in different subgroups analyzed, e.g. subjects with prior therapy. Although disease activity was high at baseline, subjects who were heavily pretreated with 1, 2 or >2 prior biologics also reached a considerable early as well as long-term efficacy under treatment with ustekinumab. This was mainly shown by the analyses of TCJ and SJC, where a constant decrease in the number of TJC during the study was observed across all subgroups by prior therapy, reaching comparable mean and median values at Week 160. Slight improvements in SJC were also seen in all subgroups by prior therapy. These ameliorations under ustekinumab treatment were also seen in other analyzed subgroups (e.g. with and without concomitant MTX treatment, subjects with axial involvement and subjects with dactylitis). Continued improvements during the study were also seen in skin results, as BSA affected and PASI.

Around 18% of subjects without MDA at baseline had reached MDA at Weeks 28 and Week 52. The median duration of MDA reached at least once during the study was 26 weeks.

Slight improvements were documented for patient reported outcomes as SF-12, NAPSI and dactylitis score. This is in agreement with a very good or good effectiveness at Week 160 assessed by most subjects and the good results of the tolerability assessments by physicians and subjects.

Ustekinumab was generally well tolerated, and the safety data observed in the study so far were consistent with the established safety profile of ustekinumab.